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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,789	09/12/2006	Hiroshi Sugiyama	Q96589	1416

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EXAMINER	
CHU, YONG LIANG	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
07/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,789	SUGIYAMA ET AL.	
	Examiner	Art Unit	
	YONG CHU	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,14,16 and 18-21* is/are rejected.

7)☒ Claim(s) *1-21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/12/2006, and 01/05/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are pending in the instant application.

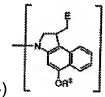
Information Disclosure Statement

Applicants' Information Disclosure Statements, filed 09/12/2006, and 01/05/2007 have been considered. Please refer to Applicant's copies of the PTO-1449 submitted herewith.

Priority

This application is 371 of PCT/JP04250 filed on 03/10/2005, which claims foreign priority of Japan Patent Application No. 2004-114793 filed 03/13/2005.

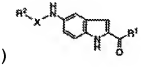
Response to Restriction/Election

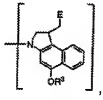
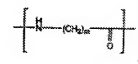
Applicant's election *without traverse* of Group II (i.e. claims 1-21) and the elected species of compound with $\mathbf{R^1}$ is formula (4)  in the reply filed 04/29/2008 is acknowledged. Since this application is a national stage of PCT application, and the way claim1 is drafted, claims 1-21 will be examined together, unless the invention is found lack of unity of invention during the examination. Accordingly, the restriction requirement dated on 02/04/2008 has hereby withdrawn.

Status of the Claims

Elected and Examined Subject Matter

The scope of the invention of the elected subject matter and the examined subject matter is as follows:

An indole derivative of formula (I)  according to claim 1, wherein:

R_1 is  , or  , and the remaining substituents are as defined in claim 1. Claim 1 defines substituent **X** as a divalent group **"having"** one constitutional unit or having two or more constitutional units represented by the three formulae according to claim 1. According to MPEP 2111.03, "having" must be interpreted in light of the specification to determine whether open or closed claim language is intended. See, e.g., *Lampi Corp. v. American Power Products Inc.*, 228 F.3d 1365, 1376, 56 USPQ2d 1445, 1453 (Fed. Cir. 2000). All the compound examples contain the only three groups as **X**:  ,  or  . Therefore, the instant transitional phrase **"having"** in claim 1 is interpreted as an –close-ended term, which include only the three units of **X** group.

As a result of the election and the corresponding scope of the invention identified supra, the remaining subject matter of claims 1-21 are withdrawn from further consideration pursuant to 37 CFR 1.142 (b) as being drawn to non-elected inventions. The withdrawn compounds or compositions contain varying functional groups which are chemically recognized to differ in structure, function, and reactivity. The scope of the invention is set in considering the elected species and the preferred embodiments. In addition, a reference, which anticipates one group, would not render obvious the other. Therefore, claims 1-21 will be examined on the merits.

Specification

Sequence Compliance

Pursuant to 37 CFR 1.821, a sequence identifier must be provided for any amino acid sequences of four or more residues or nucleotide sequences of 10 or more nucleotides. The following omissions have been identified in the specification and the sequences do not appear in the Sequence Listing:

SEQ ID NO: 1-19, p. 35-37.

Applicants will need to provide a Sequence Listing, a computer readable form of the Sequence Listing and a statement. Please see the attached Notice to Comply Form, for which the Examiner has set a 3-month shortened statutory period for response.

The first paragraph of the specification does not contain continuing data to which the instant specification claims benefit from. An appropriate amendment is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. More specifically, claims 18-21 claim a drug containing an instantly claimed compound of claim 1 for suppressing or activating the expression of a gene, or, an abnormal gene, a SNP gene, or an oncogene. By definition, a gene is a locatable region of genomic sequence, corresponding to a unit of inheritance, which is associated with regulatory regions, transcribed regions and/or other functional sequence regions. The estimated number of genes in the human genome is estimated about 20,000–25,000 protein-coding genes, with an article from 2007 giving a number of 20,488, plus perhaps 100 more yet to be discovered, see *Wikipedia under "Gene"*. However, the instant specification discloses a compound against human ER(+) breast cancer Br-10 in vivo only, but fails to describe the other oncogene, or SNP gene, or how to suppress or activates any gene expression.

Claims 18-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling as a compound to suppress human ER(+) breast cancer Br-10, but fails to describe how the instantly claimed drug containing the claimed compound for suppressing or activating the other oncogene, SNP gene, or any gene expression. The instant enablement rejection is on two grounds: first, as being claimed as a drug, especially is being used for treating diseases such as cancer, it is regulated by FDA. To be marketed as a drug, a chemical compound or a composition has to go through phase I-III of clinical trial under the FDA guidelines for safety and efficacy evaluations, and the outcome is very unpredictable. The instant application fails to demonstrate how to get the claimed composition approved by FDA for being used as drug. Second, many genes are responsible for each type of cancer, and oncogene is a general term of all the genes which cause cancers, such as lung cancer, colon cancer, liver cancer, breast cancer, etc. The instant application fails to teach one skilled in the art how to use the claimed composition or "drug" to suppress or activate a gene. The instant claims 18-21 fail at the both grounds on teaching how to use the claims, and therefore, fail to comply with the enablement requirement.

Claim Rejections - 35 USC § 103(a)

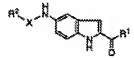
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

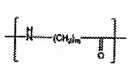
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

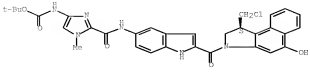
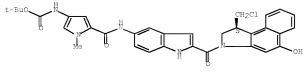
Claims 1-3, 14, and 16 are rejected under 35 U.S.C. 103 (a) as unpatentable over PCT publication WO2003022806 (equivalent U.S. Publication No. US20050014700) by Boger et al. ("the `806 publication") in view of U.S. Patent No. 5,843,937 by Wang et al. ("the 937 patent"), U.S. Patent No. 6,281,354 by Boger et al. ("the `354 patent"), and Boger et al. , *J. Org. Chem.*, **2001**, 66, p.6654-6661.

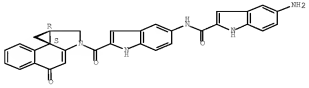
Applicants' claims relate to an indole derivative of formula (I) 

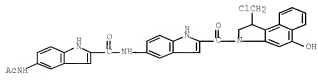
according to claim 1, wherein:

R_1 is  , or  , **X** is a repeating unit of independently selected from  ,  , and  , and the remaining substituents are as defined in claim 1, or an alkylating agent comprising said compound.

Determination of the scope and content of the prior art (MPEP §2141.01)

The `806 publication discloses a class of compounds for sequence selective alkylation of duplex DNA, and used as anticancer agents. More specifically, the compounds  (CAS RN 372954-19-3) and  (CAS RN 372954-20-6) is disclosed in the publication.

The `354 patent discloses a class of compounds for sequence selective alkylation of duplex DNA, and used as anticancer agents. More specifically, the compound  (CAS RN 216298-83-8) is disclosed in the patent.

The `937 patent discloses compounds for sequence selective alkylation of duplex DNA, and used as anticancer agents. More specifically, the compound  (CAS RN 199806-33-2) is disclosed in the patent.

Boger et al. teaches the DNA alkylation rate and efficiency increase about 10,000-fold, and the resulting biological activity also increase by 10,000-fold when

simple N-acetyl or N-Boc derivatives of the alkylation subunits, which lack the DNA-binding domain.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the `806 compounds and the instantly claimed compounds is that the prior art compounds have R^2 as N-Boc group, and the instantly claimed compounds have R^2 as hydrogen, an alkyl, or an acyl.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

However, such difference would have been obvious to one ordinary skilled in the art in view the teaching by the `354 patent and/or the `937 patent. The `354 patent teaches a very similar compound with $R^2$ as hydrogen, and the `937 patent teaches a very similar compound with R^2 as acyl group, and Boger et al. teaches the DNA alkylation rate and efficiency increase about 10,000-fold, and the resulting biological activity also increase by 10,000-fold when simple N-acetyl or N-Boc derivatives of the alkylation subunits. Furthermore, all the compounds taught in the prior arts have very similar core structure, and is used for the same utility, namely, alkylating a DNA sequence with anti-cancer activity. The motivation to make the claimed compounds from the prior art teaching derives from the expectation that structurally similar compounds would possess similar activity (i.e. pharmacological use). Therefore, the instantly claimed compounds would have been suggested to one skilled in the art.

Claim Objection

Claims 1-3, and 14-21 are objected to for containing elected and non-elected subject matter. The elected subject matter has been identified supra.

Claims 4-13 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

- Specification is objected to.
- Claims 1-21 are objected to.
- Claims 1-3, 14, 16, and 18-21 are rejected.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Status Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong Chu, Ph.D./
Patent Examiner
Art Unit 1626